

CLAIMS

1. A fusion gene comprising a cell death-inducing gene that acts specifically on a surface receptor of endothelial cells undergoing angiogenesis, wherein the fusion gene is produced by fusing, a gene that codes for a homing signal peptide sequence specific for the surface receptor of endothelial cells undergoing angiogenesis, a gene coding for green fluorescent protein (GFP) and a gene coding for Δ NBax protein, which is human Bax with a deletion of the N-terminal sequence including the BH3 domain, in this order.
2. The fusion gene according to claim 1, wherein the homing signal peptide sequence is selected from the group consisting of peptide sequences of (a) to (o) shown below:
 - (a) RGD peptide sequence,
 - (b) NGR peptide sequence,
 - (c) peptide sequence shown in SEQ ID NO: 7,
 - (d) peptide sequence shown in SEQ ID NO: 8,
 - (e) peptide sequence shown in SEQ ID NO: 9,
 - (f) peptide sequence shown in SEQ ID NO: 10,
 - (g) peptide sequence shown in SEQ ID NO: 11,
 - (h) peptide sequence shown in SEQ ID NO: 12,
 - (i) peptide sequence shown in SEQ ID NO: 13,
 - (j) peptide sequence shown in SEQ ID NO: 14,
 - (k) peptide sequence shown in SEQ ID NO: 15,
 - (l) peptide sequence shown in SEQ ID NO: 16,
 - (m) peptide sequence comprising LDV,
 - (n) peptide sequence shown in SEQ ID NO: 17 and
 - (o) peptide sequence shown in SEQ ID NO: 18.
3. The fusion gene according to claim 2, wherein the homing signal peptide sequence is RGD or NGR which is a homing signal peptide specific for endothelial cells undergoing angiogenesis.

4. The fusion gene according to any one of claims 1-3, wherein the Δ NBax protein, which is human Bax with a deletion of the N-terminal sequence containing the BH3 domain, comprises an amino acid sequence from the 112th to 192nd of the human BAX amino acid sequence.
5. The fusion gene according to any one of claims 1-3, wherein the fusion gene comprises following DNA of (p) or (q),
 - (p) a DNA having a nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 5.
 - (q) a DNA which hybridizes with a DNA having a complementary sequence of the DNA of (p) under a stringent condition and which codes for a protein which binds to endothelial cells undergoing angiogenesis and which has an enhanced cell death-inducing activity.
6. An expression vector containing the fusion gene according to any one of claims 1 to 5.
7. The expression vector according to claim 6, which can express the fusion gene in a cell-free system.
8. A method for producing the fusion protein encoded by the fusion gene according to any one of claims 1 to 5, including a step of *in vitro* expression by the expression vector according to claim 7.
9. A fusion protein containing a cell death-inducing protein that acts specifically on surface receptor of endothelial cells undergoing angiogenesis, wherein the fusion protein is generated by fusing, a homing signal peptide sequence specific for a surface receptor of endothelial cells undergoing angiogenesis, green fluorescent protein (GFP) and Δ NBax protein, which is human Bax with a deletion of the N-terminal sequence containing the BH3 domain, in this order.

10. The fusion protein according to claim 9, wherein the homing signal peptide sequence is selected from the group consisting of peptide sequences of (a) to (o) shown below:

- (a) RGD peptide sequence,
- (b) NGR peptide sequence,
- (c) peptide sequence shown in SEQ ID NO: 7,
- (d) peptide sequence shown in SEQ ID NO: 8,
- (e) peptide sequence shown in SEQ ID NO: 9,
- (f) peptide sequence shown in SEQ ID NO: 10,
- (g) peptide sequence shown in SEQ ID NO: 11,
- (h) peptide sequence shown in SEQ ID NO: 12,
- (i) peptide sequence shown in SEQ ID NO: 13,
- (j) peptide sequence shown in SEQ ID NO: 14,
- (k) peptide sequence shown in SEQ ID NO: 15,
- (l) peptide sequence shown in SEQ ID NO: 16,
- (m) peptide sequence comprising LDV,
- (n) peptide sequence shown in SEQ ID NO: 17 and
- (o) peptide sequence shown in SEQ ID NO: 18.

11. The fusion protein according to claim 10, wherein the homing signal peptide sequence is RGD or NGR which is a homing signal peptide sequence specific for endothelial cells undergoing angiogenesis.

12. The fusion protein according to claim 10 or 11, wherein Δ NBax protein, which is human Bax with a deletion of the N-terminal sequence containing the BH3 domain, consists of an amino acid sequence from the 112th to 192nd of the human BAX amino acid sequence.

13. The fusion protein according to any one of claims 10 to 12 shown in (r) or (s) below,

(r) a fusion protein having an amino acid sequence which is represented by SEQ ID NO: 4 or 6,

(s) a protein, which has the amino acid sequence of (q) in which one or some amino acids are deleted, substituted or added, and which binds to endothelial cells undergoing angiogenesis and has enhanced cell death-inducing activity.

14. A cancer cell growth inhibitor containing the fusion protein according to any one of claims 10 to 13.

15. The cancer cell growth inhibitor according to claim 14, wherein the cell death-inducing activity of Δ NBax protein, which is human Bax with a deletion of the N-terminal sequence containing the BH3 domain, is enhanced by fusion with green fluorescent protein (GFP) as compared with that of Δ NBax protein, which is human Bax with only the N-terminal sequence containing the BH3 domain deleted.